10/516293

Translation

PCT Application
PCT/JP2003/00

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A31363M	FOR FURTHER ACTION	See Notification of Transmittal of International Prelir Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP03/07128	International filing date (*day/month/year*) 05 June 2003 (05.06.03)	Priority date (*day/month/year*) 11 June 2002 (11.06.02)

International Patent Classification (IPC) or national classification and IPC
A61K31/167, 31/17, 31/18, 31/235, 31/277, 31/381, 31/40, 31/402, 31/404, 31/415, 31/4164, 31/421, 31/422, 31/426, 31/427, 31/433, 31/437, 31/44, 31/4406, 31/4418, 31/445, 31/4453, (see supplemental sheet)

Applicant
INSTITUTE OF MEDICINAL MOLECULAR DESIGN. INC.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have bee amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rul 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 05 June 2003 (05.06.03)	Date of completion of this report 05 November 2003 (05.11.2003)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/07128

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1- a part of 12

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-12 are so unclear that no meaningful opinion could be formed *(specify)*:

The active ingredients of the medicinal compositions described in the inventions of claims 1-12 include an extremely wide and varied range of compounds, and it is impossible to conduct a complete search of them all. On the other hand, only a small portion of the active ingredients of the medicinal compositions described in the inventions of claims 1-12 are supported by the Specification in the sense of PCT Article 6 and fully disclosed in the Specification in the sense of PCT Article 5.

Therefore, the descriptions of the inventions of claims 1-12 and the Specification do not satisfy the requirement for specificity such that a meaningful international search can be conducted.

As a result, in this international examination report a search of prior art was conducted for the inventions of claims 1-12 within a reasonable scope based on the compounds that are specifically disclosed in the Specification, and this international preliminary examination will be conducted within the scope of that search.

☒ the claims, or said claims Nos. 1-12 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1- a part of 12

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/07128

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1- a part of 12

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-12 are so unclear that no meaningful opinion could be formed *(specify)*:

The active ingredients of the medicinal compositions described in the inventions of claims 1-12 include an extremely wide and varied range of compounds, and it is impossible to conduct a complete search of them all. On the other hand, only a small portion of the active ingredients of the medicinal compositions described in the inventions of claims 1-12 are supported by the Specification in the sense of PCT Article 6 and fully disclosed in the Specification in the sense of PCT Article 5.

Therefore, the descriptions of the inventions of claims 1-12 and the Specification do not satisfy the requirement for specificity such that a meaningful international search can be conducted.

As a result, in this international examination report a search of prior art was conducted for the inventions of claims 1-12 within a reasonable scope based on the compounds that are specifically disclosed in the Specification, and this international preliminary examination will be conducted within the scope of that search.

☒ the claims, or said claims Nos. 1-12 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1- a part of 12

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No. PCT/JP03/07128

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	8-10	YES
	Claims	1-7, 11-12	NO
Inventive step (IS)	Claims		YES
	Claims	1-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO

2. Citations and explanations

Document 1: WO 01/98290 A1 (PARMACIA & UPJOHN S.P.A.) December 27, 2001
Document 2: EP 1205478 A1 (TAKEDA CHEMICAL INDUSTRIES) May 15, 2002
Document 3: DUMAS, J., "Synthesis and structure-activity relationships of novel small molecule cathepsin D inhibitors," Bioorganic & Medicinal Chemistry Letters (1999), Vol. 9, No. 17, pp. 2531-2536
Document 4: WO 93/24115 A1 (MCGEER, P. L.) December 9, 1993
Document 5: WO 99/24404 A1 (AMGEN INC.) May 20, 1999
Document 6: WO 96/17832 A1 (WARNER-LAMBERT CO.) June 13, 1996
Document 7: UPADHAY P., "Synthesis and pharmacological evaluation of some new imidazolinones as anticonvulsants," Indian Journal of Heterocyclic Chemistry (1991), Vol. 1, No. 2, pp. 71-74
Document 8: LADVA, K., "Oxadiazoles. Part XV. Synthesis and biological activities of substituted 1,3,4-oxadiazole derivatives," Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1996), Vol. 35B, No. 10, pp. 1062-1066
Document 9: EP 483881 A1 (MERRELL DOW PHARMACEUTICALS, INC.), May 6, 1992
Document 10: WO 98/20864 A2 (UNIVERSITA' DEGLI STUDI DI BRESCIA-DIPARTIMENTO DI SCIENZE BIOMEDICHE) May 22, 1998
Document 11: WO 99/65449 A2 (SMITHKLINE BEECHAM CORPORATION) December 23, 1999
Document 12: WO 00/03991 A1 (TAKEDA CHEMICAL INDUSTRIES) January 27, 2000
Document 13: US 4661630 A (EIZAI CO., LTD.) April 28, 1987

[1] Based on the descriptions in documents 1-6 cited in the international search report, the inventions of claims 1 and 3-7 lack novelty and an inventive step.

Documents 1-6 state that compounds corresponding to General Formula (I) are useful in the treatment of Alzheimer's disease (see document 1 pages 48 and 57, document 2 pages 70 and 104, document 3 page 2534, document 4 page 12, document 5 pages 51 and 247, document 6 pages 2 and 27).

Among the compounds corresponding to General Formula (I), documents 1-6 describe those in which A is a hydrogen atom, and documents 1-3 describe those in which the group corresponding to ring Z is a benzene ring with a halogen substituent (see locations noted above). In addition, document 5 lists a naphthyl as a group corresponding to ring Z (see document 5, page 244).

In addition, these documents describe a five-member heteroaryl group as a group corresponding to ring E (see documents 1, 2, 4, and 5, etc.).

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 02/49632 A1 (Institute of Medicinal Molecular Design Inc.) [EX]	27.06.02	18.12.01	18.12.00

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

[2] Based on the descriptions in documents 6-10 cited in the international search report, the inventions of claims 2-5 and 7 lack novelty and an inventive step.

Documents 6-10 state that compounds corresponding to General Formula (I) are useful in the treatment of epilepsy (see document 6, pages 2 and 27, document 7 pages 71-74, document 8 pages 1062-1066, document 9 pages 15 and 89, document 10 page 17).

Among the compounds corresponding to General Formula (I), documents 6-10 describe those in which A is a hydrogen atom, and documents 7 and 8 describe those in which the group corresponding to ring Z is a naphthyl group. In addition, document 8 describes one in which the group corresponding to ring Z may be substituted by a halogen (see locations noted above).

In addition, these documents describe a five-member monocyclic heteroaryl group as a group corresponding to ring E (see documents 7, 8, and 10, etc.).

[3] Based on the description in documents 11, 12, and 13 cited in the international search report, the inventions of claims 8-10 lack an inventive step.

Document 11 states that compounds having a phenyl amide as a basic scaffold are useful in the treatment of Alzheimer's disease and epilepsy (pages 23-27). These differ however, from the inventions of claims 8-10, which have trifluoromethyl 3,5-disubstituted phenyl group as ring E.

However, document 11 lists a hydrocarbon group and halogen, etc., as a substituent of the phenyl group that is adjacent to the amide. Documents 12, and 13 each describe compounds that have the same phenyl amide scaffold and are trifluoromethyl 3,5-disubstituted as compounds that are useful for the treatment of Alzheimer's disease and epilepsy (see document 12, pages 26-32, document 13, columns 3 and 4).

This being the case, persons skilled in the art can easily select trifluoromethyl 3,5-disubstitution on the benzene ring adjacent to the amide in the compound described in document 11.

In addition, this examination finds that the selection of these substituents does not provide any particularly outstanding, unforeseen effect.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box :

Continuation of International Patent Classification (IPC)

31/451, 31/454, 31/47, 31/496, 31/4965, 31/498, 31/505, 31/5375, 31/5377, 31/695,
A61P25/08, 25/28, 43/00